REMARKS

Claims 1-9 and 11-20 are pending in the instant application. Claims 1-9 and 11-20 have been rejected. Claims 1 and 16 have been amended. Support for these amendments is provided in claim 12, now canceled. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of the following remarks.

Rejection of Claims 1-9 and 11-20 under 35 U.S.C. 103(a)

Claim 20 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Modamio et al. (Int. J. Pharmaceutics 1998 173:141-148) in view of Hirano et al. (U.S. Patent 6,495,159). The rejection of claims 1-9 and 11-19 under 35 U.S.C. 103(a) as being unpatentable over Modamio et al. (Int. J. Pharmaceutics 1998 173:141-148) in view of Hirano et al. (U.S. Patent 6,495,159) and Higo et al. (U.S. Patent 5,866,157) further evidenced by Walters (Transdermal Drug Delivery, 1989, New York, NY, pp 97-246), has also been maintained.

Applicants respectfully traverse these rejections.

At the outset, it is respectfully pointed out that claim 1 has been amended to be drawn to an adhesive patch having a pressure-sensitive adhesive layer comprising

bisoprolol and/or a pharmaceutically acceptable salt thereof, wherein the composition of pressure-sensitive adhesive layer contains an acrylic polymer obtained by copolymerizing a (meth)acrylic ester with a (meth)acrylic acid comprising a carboxyl group and wherein the penetration rate of bisoprolol through skin is 3-300 $\mu g/h \cdot cm^2$. Support for this amendment is provided in claim 12, now canceled.

The cited combination of references does not teach the claimed invention as a whole as required to establish obviousness of the invention. See MPEP 2141.

As acknowledged by the Examiner, Modamio does not expressly disclose a patch containing bisoprolol. Modamio also provides no teaching or suggestion of an adhesive layer containing an acrylic polymer obtained by copolymerizing a (meth)acrylic ester with a (meth)acrylic acid comprising a carboxyl group. Further, Modamio does not teach a penetration rate of bisoprolol of 3-300 $\mu g/h \cdot cm^2$. In fact, Modamio suggests difficulties in providing a therapeutically effective penetration rate of bisoprolol. See Abstract of Modamio which teaches that both, referring to celiprolol and bisoprolol, provide plasma concentrations at steady state that would be far from their therapeutic concentrations.

Teachings of Hirano and Higo fail to remedy the deficiencies in Modamio.

Applicants respectfully disagree with the Examiner's suggestion that the 2-ethylhexyl acrylate/ethylacrylate-vinyl acetate copolymer taught in Example 2 of Hirano is structurally similar to the acrylic polymer of claims 3, 4 and 15 of the instant application. Claims 3, 4 and 15 depend from claim 1 wherein it is explicitly stated that the (meth)acrylic acid comprises a carboxyl group. 2-Ethylhexyl acrylate/ethylacrylate-vinyl acetate copolymer of Example 2 of Hirano does not comprise a carboxyl group. Instead of being structurally similar to the instant claimed acrylic polymer as suggested by the Examiner, 2-ethylhexyl acrylate/ethylacrylate-vinyl acetate copolymer of Example 2 of Hirano is similar to 2-ethylhexyl acrylate/vinyl acetate copolymer used in the patch of Comparative Example 2 of the instant specification which exhibited unfavorable adhesive properties and drug content stability compared to a patch comprising a (meth)acrylic ester with a (meth)acrylic acid comprising a carboxyl group as claimed.

Applicants also respectfully disagree with the Examiner's characterization of Hirano as teaching a patch that possesses a backing layer which is in direct contact

with the pressure sensitive adhesive layer as recited in claim 20. Hirano describes a percutaneous therapeutic apparatus comprising a backing layer, wherein the backing layer is defined as one of the most outer layers (see Fig 1-1 and claim 1). There is at least a medicine storage layer between said backing layer and pressure sensitive adhesive layer, and is some cases a medicine permeable layer as well. Further, Hirano describes a press layer 6 along the periphery of the effective releasing surface at the portion wherein the medicine permeable film and the backing material are sealed in order to seal the medicine storage layer (see col. 3, lines 54-60) so that again, said backing layer is not in contact with the pressure sensitive adhesive layer as claimed in the instant application.

Accordingly, combined teachings of Modamio and Hirano, when read as a whole, clearly do not result in the instant claimed invention.

Combining Higo also fails to remedy deficiencies as this reference does not teach a patch using an acrylic polymer. Nor does this reference provide any suggestion of using an acrylic polymer obtaining by copolymerizing a (meth)acrylic ester with a (meth)acrylic acid comprising a carboxyl group as claimed in the instant application.

Further, neither the Hirano reference nor the Higo reference, which are unrelated to bisoprolol, provide any reasonable expectation of success with respect to successful percutaneous administration of this drug at a penetration rate of bisoprolol through skin of 3-300 $\mu g/h \cdot cm^2$ as claimed, particularly in light of teachings of Modamio that plasma concentrations at steady state are far from their therapeutic concentrations.

Accordingly, the cited combination of references fail to suggest the desirability and thus the obviousness of making the instant claimed invention and provide no reasonable expectation of success with respect to the instant claimed invention.

Withdrawal of this rejection under 35 U.S.C. 103(a) is therefore respectfully requested.

Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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